

Appl. No. 10/815,727  
Response dated November 14, 2005  
Reply to Office action of July 13, 2005

**Amendments to the Drawings**

Please replace Figure 20 and Figure 22 currently of record with Replacement Figure 20 and 22, respectively, submitted herewith.

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### REMARKS/ARGUMENTS

#### Claim Amendments

By the present amendment, claim 1 has been amended to incorporate the subject matter of claim 2. Accordingly, claim 2 has been cancelled.

Claim 3 has been amended to change its dependency from claim 2 to claim 1 since claim 2 has been cancelled.

Claim 5 has been amended to remove the word "a" preceding the expression "dextran-based silane", as requested by the Examiner.

Claim 10 has been amended to replace the word "lipid" with the word "phospholipid" to correct antecedent inconsistencies. The word "phospholipid" finds antecedent basis in claim 9.

Claims 11 and 25 have been amended to remove the word "about" as requested by the Examiner.

Claim 12 has been amended to replace the expression "optionally comprising an effective amount of a humectant" with "wherein the aqueous buffer optionally comprises an effective amount of a humectant". This is a clarifying amendment that does not alter the scope of claim 12 in any way.

Claim 15 has been corrected by adding the word "of" following the word "presence". This amendment corrects a typographical error and in no way alters the scope of claim 15 in any way.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been entered by the present amendment and entry of the amendments is respectfully requested.

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### **Drawing Amendments**

By the present amendment, Figure 20 has been corrected to add labels for the x-axis. Accordingly, the first bar has been labeled as "Receptor-Specific Binding" and the second bar has been labeled as "Non-specific Binding". Support for this amendment is found on page 10, lines 23-25, of the application as filed.

Figure 22 has been amended to move the x-axis labels so that they are not overlapping the bar graph as requested by the Examiner.

The Applicants submit that no new matter has been added to the figures as a result of these amendments and the amendments are fully supported by the application as filed. Entry of the figure amendments is respectfully requested.

The Official Action dated July 13, 2005 has been carefully considered. It is believed that the claims and figures submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

### **Drawings**

The Examiner has objected to the drawings because Figure 20 is missing an x-axis label and Figure 22 has the x-axis label overlapping the bar graph. In Response, the Applicants have submitted herewith replacement pages for Figures 20 and 22 with appropriate corrections made to overcome the Examiner's objections. Specifically, Figure 20 has been corrected to label the first bar as "Receptor-Specific Binding" and the second bar as "Non-specific Binding". Support for these labels is found on page 10, lines 23-25, of the application as filed. Further, Figure 22 has been amended to move the x-axis labels so that they are not overlapping the bar graph as requested by the Examiner.

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In light of the above amendments, the Applicants respectfully request that the Examiner's objections to the drawings be withdrawn.

### **Claim Objections**

The Examiner has objected to claim 5 because the word "a" in line 3 should be deleted and to claim 15 because the word "of" is needed following the word "presence" in line 2. In response, the Applicants have made these corrections.

In light of the above amendments, the Applicants request that the Examiner's objections to claims 3 and 15 be withdrawn.

### **Claim Rejections**

#### **35 USC §112, Second Paragraph**

The Examiner has rejected claim 10 under 35 USC §112, second paragraph, as the limitation "the lipid" has insufficient antecedent basis. In response, the Applicants have amended claim 10 to replace the word "lipid" with the word "phospholipids". The word "phospholipid" finds antecedent basis in claim 9.

In light of the above amendment, the Applicants request that the Examiner's rejection of claim 10 under 35 USC §112, second paragraph, be withdrawn.

The Examiner has rejected claim 11 under 35 USC §112, second paragraph, as the Examiner contends that the word "about 4-11.5" in lines 5-6 is vague and indefinite. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have removed the word "about" from the above noted expression.

In light of the above amendment, the Applicants request that the Examiner's rejection of claim 11 under 35 USC §112, second paragraph, be withdrawn.

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The Examiner has rejected claim 12 under 35 USC §112, second paragraph, as the Examined contends that the phrase "optionally comprising" is vague and indefinite as it is not clear whether a humectant should be present in the aqueous buffer. In response, Claim 12 has been amended to replace the expression "optionally comprising an effective amount of a humectant" with "wherein the aqueous buffer optionally comprises an effective amount of a humectant". This amendment serves to clarify that the aqueous buffer may optionally comprise an effective amount of a humectant which overcomes the Examiner's rejection.

In light of the above amendment, the Applicants request that the Examiner's rejection of claim 12 under 35 USC §112, second paragraph, be withdrawn.

The Examiner has rejected claim 25 under 35 USC §112, second paragraph, as the Examined contends that the word "about 4-227" in line 4 is vague and indefinite. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have removed the word "about" from the above noted expression.

In light of the above amendment, the Applicants request that the Examiner's rejection of claim 25 under 35 USC §112, second paragraph, be withdrawn.

### **35 USC §102(b)**

The Examiner has rejected claims 1, 7, 9 and 11 under 35 USC §102(b) as being anticipated by Stowell et al. (U.S. Patent No. 6,284,163). In response the Applicants have incorporated the subject matter of claim 2 into claim 1, and accordingly into claims 7, 9 and 11, dependent on claim 1, which overcomes the Examiner's objection.

In light of the above amendment, the Applicants request that the Examiner's rejection of claims 1, 7, 9 and 11 under 35 USC §102(b) be withdrawn.

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The Examiner has rejected claims 1-4, 7, 11 and 14-19 under 35 USC §102(b) as being anticipated by Gill (Chem. Mater. Web Release Date of July 4, 2001, 13:3404-3421).

The Examiner contends that Gill anticipates the above claims by teaching a method of immobilizing membrane-associated molecules in silica matrixes comprising combining a liposome-assembly, which includes the membrane associated molecule, with a protein and membrane compatible sol-gel precursor under conditions to allow a gel to form. As noted above, the Applicants have amended claim 1 to incorporate the subject matter of claim 2, accordingly the claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate.

With respect to claims 2-4, the Examiner contends that Gill teaches, at page 3407, Figure 1, a method of immobilizing membrane-associated molecules in silica matrixes, wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane. The Applicants respectfully disagree with the Examiner's interpretation of Gill. Figure 1 in Gill is a summary of all of the general protocols that have been reported in the literature for sol-gel encapsulation (see Figure 1, caption). The Applicants submit that there is **no specific teaching of a membrane-associated molecule in combination with an organic polyol silane precursor in Figure 1**. Figure 1 only refers to "Biomolecule" as the species for entrapment. There is no specific reference to membrane-associated biomolecules. Further, the Applicants submit that Figure 1 does not specifically describe combining **organic-polyol silanes** with any biomolecule. Figure 1 refers to the combination of alkoxy silanes with glycerol in a transesterification reaction followed by partial hydrolysis. This produces poly(glyceryl silicate) which is a partially hydrolyzed and polycondensed precursor. It is this species that is combined with the biomolecule in the encapsulation reaction. The Applicants further submit that there is no other teaching in Gill of the specific combination of a membrane-associated molecule and an organic polyol silane precursor. Accordingly, the specific combination of an organic polyol silane precursor

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with a membrane-associated molecule is not taught in Gill and claims 3-4 are not anticipated by this reference.

With respect to claim 7, the Examiner contends that Gill teaches, in Table 4 on page 3415, a method of immobilizing membrane associated molecules in silica matrixes, wherein the membrane-associated molecule is bacteriorhodopsin. The Applicants respectfully point out that the sol-gel precursor used for the entrapment of bacteriorhodopsin reported in Table 4 is tetramethylorthosilicate (TMOS) which is not an organic polyol silane or sodium silicate and therefore does not meet the limitations of claim 7 which is dependent on claim 1. Accordingly, claim 7 is not anticipated by Gill.

With respect to the Examiner's objections to claims 11 and 14-19, the Applicants note that all of these claims are also dependent on claim 1. As argued above, the Applicants submit that claim 1 is not anticipated by Gill and therefore, claims 11 and 14-19 are, likewise, not anticipated by Gill.

In light of the above amendment and arguments, the Applicants request that the Examiner's rejection of claims 1-4, 7, 11 and 14-19 under 35 USC §102(b) be withdrawn.

The Examiner has rejected claims 1, 6, 9 and 14 under 35 USC §102(a) as being anticipated by Besanger et al. (J. Phys. Chem. B. Published on Web Sept. 20, 2002, 106:10535-10542). The Applicants respectfully submit that Besanger et al. is not a proper citation under 35 USC §102(a). The present application claims priority from U.S. provisional patent application S.N. 60/426,018 filed on November 14, 2002. It is clear that Besanger et al. is a publication that was made by the Applicant and therefore was not published by another and is not citable against the present application under 35 USC §102(a). Applicants are providing herewith a Declaration under 37 CFR §1.132 in support of this submission. The Applicants further note that Besanger et al. was published less than one year before the effective filing date of the present application and therefore is also not citable under 35 USC §102(b).

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In light of the above, the Applicants request that the Examiner's rejection of claims 1-6, 9 and 14 under 35 USC §102(a) be withdrawn.

### 35 USC §103(a)

The Examiner has rejected claim 8 under 35 USC §103(a) as being obvious in light of Besanger et al. (J. Phys. Chem. B. Published on Web Sept. 20, 2002, 106:10535-10542) in view of Stowell (U.S. Patent No. 6,284,163). As noted above, the Applicants submit that Besanger et al. is not citable against the present application, accordingly we request that the Examiner's rejection of claim 8 under 35 USC §103(a) be withdrawn.

The Examiner has rejected claim 10 under 35 USC §103(a) as being obvious in light of Stowell (U.S. Patent No. 6,284,163) in view of Dattagupta (U.S. Patent No. 5,711,964). In response, the Applicants have amended claim 1, and accordingly claim 10 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. Stowell teaches the use of silyl lipids as precursor molecules in the formation of bilayer or multilayer structures as well as in the formation of encapsulation material. Dattagupta does not describe the encapsulation of any biomolecule in sol gel matrixes. Accordingly, neither Stowell or Dattagupta teach, or even remotely suggest, the incorporation of membrane-associated molecules in sol-gel materials derived from organic polyol silanes or sodium silicate as required by claim 10 submitted herewith. In light of the above arguments the Applicants request that the Examiner's objection to claim 10 under 35 USC §103(a) be withdrawn.

Claim 10 has also been rejected under 35 USC §103(a) as being obvious in light of Besanger et al. in view of Dattagupta. As noted above, the Applicants submit that Besanger et al. is not citable against the present application, accordingly we request that the Examiner's rejection of claim 10 under 35 USC §103(a) be withdrawn.



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Claims 12 and 13 have been rejected under 35 USC §103(a) as being obvious in light of Stowell in view of Lapidot et al. (U.S. Application Publication No. US 2002/0064541, published May 30, 2002) and Smith et al. (J. Am. Chem. Soc. Published on the Web March 28, 2002). In response, the Applicants have amended claim 1, and accordingly claims 12 and 13 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. The Applicants submit that none of Stowell, Lapidot et al. or Smith et al. teach, or even remotely suggest, the incorporation of membrane-associated molecules in sol-gel materials derived from organic polyol silanes or sodium silicate as required by claims 12 and 13 submitted herewith. In light of this, the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 USC §103(a), in light of Stowell in view of Lapidot et al., be withdrawn.

The Examiner has also rejected claims 12 and 13 under 35 USC §103(a) as being obvious in light of Gill (Chem. Mater. Web Release Date of July 4, 2001, 13:3404-3421) in view of Lapidot et al. and Smith et al. In response, the Applicants have amended claim 1, and accordingly claims 12 and 13 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. As argued above, the Applicants submit that Gill does not teach nor remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. The Applicants further submit that Lapidot et al. and Smith et al. also do not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. In light of the above the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 USC §103(a), in light of Gill in view of Lapidot et al. and Smith et al., be withdrawn.

The Examiner has rejected claims 20 and 21 under 35 USC §103(a) as being obvious in light of Gill in view of Keeling-Tucker et al. (Chem. Mater. Published on Web July 31, 2001, 13:3331-3350). In response, the Applicants have amended claim 1, and

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accordingly claims 20 and 21 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. As argued above, the Applicants submit that Gill does not teach nor remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. The Applicants further submit that Keeling-Tucker et al. also does not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. In light of the above the Applicants request that the Examiner's rejection of claims 20 and 21 under 35 USC §103(a) be withdrawn.

The Examiner has rejected claims 20-23 under 35 USC §103(a) as being obvious in light of Gill in view of Leung et al. (U.S. Patent No. 6,204,202, March 20, 2001). In response, the Applicants have amended claim 1, and accordingly claims 20-23 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. As argued above, the Applicants submit that Gill does not teach nor remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. The Applicants further submit that Leung et al. also does not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. In light of the above the Applicants request that the Examiner's rejection of claims 20-23 under 35 USC §103(a) be withdrawn.

Claims 24 and 25 have been rejected under 35 USC §103(a) as being obvious in light of Gill in view of Delamarche et al. (Langmuir, Published on Web September 11, 2003, 19:8749-8758). In response, the Applicants have amended claim 1, and accordingly claims 24 and 25 dependent thereon, so that these claims are directed to methods wherein the protein- and membrane-compatible sol-gel precursor is an organic polyol silane or sodium silicate. As argued above, the Applicants submit that Gill does not teach nor remotely suggest the encapsulation of membrane-associated molecules in

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sol-gel materials prepared from polyol-modified silanes or sodium silicate. The Applicants further submit that Delamarche et al. also does not teach or remotely suggest the encapsulation of membrane-associated molecules in sol-gel materials prepared from polyol-modified silanes or sodium silicate. In light of the above the Applicants request that the Examiner's rejection of claims 24 and 25 under 35 USC §103(a) be withdrawn.

### Double Patenting

The Examiner has provisionally rejected claims 1-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 15, 16, 37-39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/647,174 in view of Gill (Chem. Mater. Web Release Date of July 4, 2001, 13:3404-3421). The Applicants wish to inform the Examiner that co-pending Application No. 10/647,174 has been abandoned for failure to respond to the outstanding Office Action which renders this provisional rejection moot. In light of this the Applicants request that the Examiner's rejection of claims 1-25 as being unpatentable over claims 1-9, 15, 16, 37-39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/647,174 in view of Gill under the judicially created doctrine of obviousness-type double patenting be withdrawn.

The Examiner has provisionally rejected claims 1-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-pending Application No. 10/814,123 in view of Gill. The Applicants respectfully traverse this rejection for the reasons that follow.

As noted on page 1, lines 19-28, of the present application as filed, molecules that are associated with membranes are less robust than their freely soluble counterparts, therefore robust and facile mobilization techniques are needed to accommodate the sensitive supramolecular assemblies of proteins, and other membrane-associated molecules, within lipid bilayers. The Applicants presented a review of methods that have been previously reported for the entrapment of membrane-associated molecules on pages 1-3 of the application as filed. The overall conclusion is

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that "[p]revious immobilization methods have been observed to reduce the natural dynamic motions of the bilayers, and lead to unstable immobilized structures" (page 2, lines 17-19). The Applicants further submit that, at the priority date of the present application, only a single membrane-associated protein had been successfully entrapped in sol-gel derived silica (page 3, lines 15-28). In this method the sol-gel was prepared using tetraethylorthosilicate (TEOS) or tetramethylorthosilicate (TMOS) and there were limitations in the ability to monitor the ion channel activity of membrane proteins entrapped therein.

The Applicants note that Gill, as a review article, reports the above entrapment of a membrane-associated molecule in sol-gel prepared from TEOS and TMOS. However, as previously argued, Gill does not report the entrapment of membrane-associated molecule in sol-gel prepared from organic polyol silanes or sodium silicate. Given the inherent difficulties that have been previously reported for the successful entrapment of membrane-associated molecules in a manner which allows them to be functionally active and which allows their activity to be monitored, there would have been no expectation of success by a person skilled in the art for the entrapment of such molecules in sol gels prepared using the precursors described in co-pending application no. 10/647,174.

The patent system is meant to foster continued innovation on original inventions. The Applicants continued to work on their original invention and found, unexpectedly, that their methods could be used to successfully entrap membrane-associated molecules and monitor their activity and therefore should be rewarded for this inventive work. Accordingly, the Applicants submit that the claims of the present invention are not obvious in light of claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-pending application no. 10/647,174 and Gill.

In light of this the Applicants request that the Examiner's rejection of claims 1-25 as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 42, 47, 49 and 51 of co-

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pending Application No. 10/814,123 in view of Gill under the judicially created doctrine of obviousness-type double patenting be withdrawn.

Early and favorable action on the merits is awaited. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is kindly requested to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

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By



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Enclosures:

Amended Figures 20 and 22  
Declaration under 37 CFR 1.132 of John D. Brennan